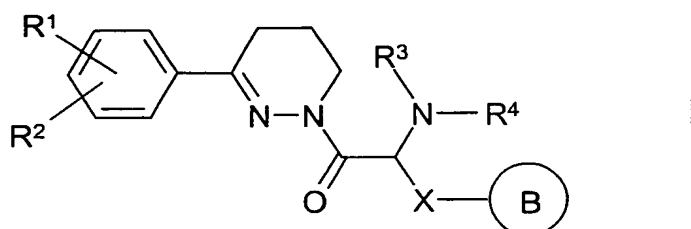


Patent Claims

1. Compounds of the formula I



5

in which

R^1 and R^2 are each, independently of one another, H, OH, OR^8 , $-SR^8$, $-SOR^8$, $-SO_2R^8$ or Hal,

R^1 and R^2 together are alternatively $-OCH_2O-$ or $-OCH_2CH_2O-$,
 R^3 is H, $A''R^9$, $COA''R^9$, $COOA''R^9$, $CONH_2$, $CONHA''R^9$,
 10 $CON(A''R^9)(A'''R^9)$, NH_2 , $NHA''R^9$, $N(A''R^9)(A'''R^9)$, $NCOA''R^9$
 or $NCOOA''R^9$,

R^4 is H, $A''R^9$, $COA''R^9$, $COOA''R^9$, $CONH_2$, $CONHA''R^9$ or
 $CON(A''R^9)(A'''R^9)$,

15 B is an aromatic isocyclic or heterocyclic radical, which may be
 unsubstituted or monosubstituted, disubstituted or trisubsti-
 tuted by R^5 , R^6 and/or R^7 ,

X is alkylene having 1-10 carbon atoms or alkenylene having
 2-8 carbon atoms,

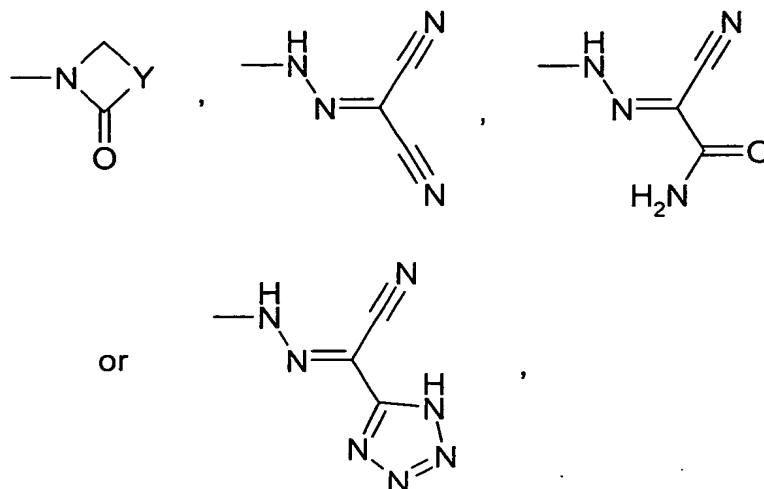
20 in which one, two or three CH_2 groups may be replaced by
 O, S, SO, SO_2 , NH or $NA''R^9$,

1-7 H atoms may be replaced by F and/or Cl,

and/or 1 or 2 H atoms may be replaced by R^{11} and/or R^{12} ,

R^5 , R^6

25 and R^7 are each, independently of one another, H, $A''R^9$, OH,
 $OA''R^9$, NH_2 , $NHA''R^9$, $N(A''R^9)(A'''R^9)$, $NHCOA''R^9$,
 $NHCOOA''R^9$, $NHCONH_2$, $NHCONHA''R^9$,
 $NHCON(A''R^9)(A'''R^9)$, Hal, $COOH$, $COOA''R^9$, $CONH_2$,
 $CONHA''R^9$, $CON(A''R^9)(A'''R^9)$,



R⁸ is A, cycloalkyl having 3-7 carbon atoms or alkylenecycloalkyl having 4-8 carbon atoms,

5 R⁹ is H, COOH, COOA, CONH₂, CONHA, CONAA', NH₂, NHA, NAA', NCOA, NCOOA, OH, OA, (CH₂)_n-aryl or (CH₂)_nHet,

R¹⁰ is alkyl having 1-10 carbon atoms, cycloalkyl having 3-7 carbon atoms, alkylenecycloalkyl having 4-8 carbon atoms or alkenyl having 2-8 carbon atoms,

10 in which one, two or three CH₂ groups may be replaced by O, S, SO, SO₂, NH, NMe, NEt and/or by -CH=CH- groups, 1-7 H atoms may be replaced by F and/or Cl, and/or 1 H atom may be replaced by R⁹,

15 R¹¹ is H, A, COOA''R⁹, CONH₂, CONHA''R⁹, CON(A''R⁹)(A'''R⁹), NH₂, NHA''R⁹, N(A''R⁹)(A'''R⁹), NCOA''R⁹, NCOOA''R⁹, OH or OA''R⁹,

R¹² is H, A, COOA''R⁹, CONH₂, CONHA''R⁹ or CON(A''R⁹)(A'''R⁹),

20 Y is alkylene having 1-10 carbon atoms or alkenylene having 2-8 carbon atoms, in which one, two or three CH₂ groups may be replaced by O, S, SO, SO₂, NH or NR¹⁰ and/or 1-7 H atoms may be replaced by F and/or Cl,

- A and A' are each, independently of one another, alkyl having 1-10 carbon atoms or alkenyl having 2-8 carbon atoms, in which one, two or three CH₂ groups may be replaced by O, S, SO, SO₂, NH or NR¹⁰ and/or
- 5 1-7 H atoms may be replaced by F and/or Cl, or aryl or Het,
- A and A' together are alternatively an alkylene chain having 2-7 carbon atoms, in which one, two or three CH₂ groups may be replaced by O, S, SO, SO₂, NH, NR¹⁰, NCOR¹⁰ or NCOOR¹⁰,
- 10 A" and A''' are each, independently of one another, absent, alkylene having 1-10 carbon atoms, alkenylene having 2-8 carbon atoms or cycloalkylene having 3-7 carbon atoms, in which one, two or three CH₂ groups may be replaced by O, S, SO, SO₂, NH or NR¹⁰ and/or
- 15 1-7 H atoms may be replaced by F and/or Cl,
- A" and A''' together are alternatively an alkylene chain having 2-7 carbon atoms, in which one, two or three CH₂ groups may be replaced by O, S, SO, SO₂, NH, NR¹⁰, NCOR¹⁰ or NCOOR¹⁰,
- 20 aryl is phenyl, naphthyl, fluorenyl or biphenyl, each of which is unsubstituted or monosubstituted, disubstituted or trisubstituted by Hal, R¹⁴, OR¹³, N(R¹³)₂, NO₂, CN, COOR¹³, CON(R¹³)₂, NR¹³COR¹³, NR¹³CON(R¹³)₂, NR¹³SO₂A, COR¹³, SO₂N(R¹³)₂ or S(O)_mR¹⁴,
- 25 R¹³ is H or alkyl having 1-6 carbon atoms,
- R¹⁴ is alkyl having 1-6 carbon atoms,
- Het is a monocyclic or bicyclic saturated, unsaturated or aromatic heterocyclic ring having 1 or 2 N, O and/or S atoms, which may be unsubstituted or monosubstituted or disubstituted by carbonyl oxygen, Hal, R¹⁴, OR¹³, N(R¹³)₂, NO₂, CN, COOR¹³, CON(R¹³)₂, NR¹³COR¹³, NR¹³CON(R¹³)₂, NR¹³SO₂R¹⁴, COR¹³, SO₂NR¹³ and/or S(O)_mR¹⁴,
- 30

Hal is F, Cl, Br or I,
m is 0, 1 or 2,
n is 0, 1, 2, 3 or 4,

and pharmaceutically usable derivatives, solvates and stereoisomers
5 thereof, including mixtures thereof in all ratios.

2. Compounds according to Claim 1, in which
R¹ and R² are each, independently of one another, H, methoxy, ethoxy,
benzyloxy, propoxy, isopropoxy, difluoromethoxy, F, Cl,
10 cyclopentyloxy, cyclohexyloxy or cycloheptyloxy,
and pharmaceutically usable derivatives, solvates and stereoisomers
thereof, including mixtures thereof in all ratios.

3. Compounds according to Claim 1, in which
15 R¹ and R² are each, independently of one another, methoxy, ethoxy,
propoxy, isopropoxy, cyclopentyloxy or F,
and pharmaceutically usable derivatives, solvates and stereoisomers
thereof, including mixtures thereof in all ratios.

20 4. Compounds according to Claim 1, in which
R¹ is 4-methoxy,
R² is 3-ethoxy,
and pharmaceutically usable derivatives, solvates and stereoisomers
thereof, including mixtures thereof in all ratios.

25 5. Compounds according to one or more of Claims 1-4,
in which
R⁴ is H,
and pharmaceutically usable derivatives, solvates and stereoisomers
30 thereof, including mixtures thereof in all ratios.

6. Compounds according to one or more of Claims 1-5,
in which

R^3 is H, $\text{COO}(\text{CH}_2)_n\text{-aryl}$, COA^{H} , COOA^{H} , $\text{A}^{\text{H}}\text{NAA}'$, $\text{A}^{\text{H}}\text{-aryl}$ or $\text{A}^{\text{H}}\text{Het}$,

and pharmaceutically usable derivatives, solvates and stereoisomers thereof, including mixtures thereof in all ratios.

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7. Compounds according to one or more of Claims 1-6, in which

X is methylene, ethylene, propylene or butylene, and pharmaceutically usable derivatives, solvates and stereoisomers thereof, including mixtures thereof in all ratios.

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8. Compounds according to one or more of Claims 1-7, in which

B is phenyl, pyridyl, pyridyl N-oxide, thienyl, furyl, pyrrolyl, pyridazinyl, pyrimidinyl, pyrazinyl, triazinyl, isoxazolinyl, oxazolinyl, thiazolinyl, pyrazolinyl, imidazolinyl, naphthyl, quinolinyl, isoquinolinyl, cinnolinyl, phthalazinyl, quinazolinyl or quinoxalinyl, each of which is unsubstituted or may be monosubstituted, disubstituted or trisubstituted by OH, OA, NH_2 , NAA' , O-alkylene- NAA' or O-alkylene-OH,

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and pharmaceutically usable derivatives, solvates and stereoisomers thereof, including mixtures thereof in all ratios.

9. Compounds according to one or more of Claims 1-8, in which

25

B is phenyl which is unsubstituted or monosubstituted by OR^{13} , $\text{N}(\text{R}^{13})_2$, O-alkylene- $\text{N}(\text{R}^{13})_2$ or O-alkylene-OH, or unsubstituted pyridyl,

and pharmaceutically usable derivatives, solvates and stereoisomers thereof, including mixtures thereof in all ratios.

30

10. Compounds according to one or more of Claims 1-9, in which

- R^1 and R^2 are each, independently of one another, H, methoxy, ethoxy, benzyloxy, propoxy, isopropoxy, difluoromethoxy, F, Cl, cyclopentyloxy, cyclohexyloxy or cycloheptyloxy,
- R^1 and R^2 together are alternatively $-OCH_2O-$ or $-OCH_2CH_2O-$,
- 5 R^3 is H, $A''R^9$, $COA''R^9$, $COOA''R^9$, $CONH_2$, $CONHA''R^9$, $CON(A''R^9)(A'''R^9)$, NH_2 , $NHA''R^9$, $N(A''R^9)(A'''R^9)$, $NCOA''R^9$ or $NCOOA''R^9$,
- R^4 is H,
- X is methylene, ethylene, propylene or butylene,
- 10 A'' and A''' are each, independently of one another, absent or alkylene having 1, 2, 3 or 4 carbon atoms,
- R^9 is H, $(CH_2)_n$ -aryl or $(CH_2)_n$ Het,
- and pharmaceutically usable derivatives, solvates and stereoisomers thereof, including mixtures thereof in all ratios.
- 15 11. Compounds according to one or more of Claims 1-10, in which
- R^1 and R^2 are each, independently of one another, H, methoxy, ethoxy, benzyloxy, propoxy, isopropoxy, difluoromethoxy, F, Cl, cyclopentyloxy, cyclohexyloxy or cycloheptyloxy,
- 20 R^1 and R^2 together are alternatively $-OCH_2O-$ or $-OCH_2CH_2O-$,
- R^3 is H, $A''R^9$, $COA''R^9$, $COOA''R^9$, $CONH_2$, $CONHA''R^9$, $CON(A''R^9)(A'''R^9)$, NH_2 , $NHA''R^9$, $N(A''R^9)(A'''R^9)$, $NCOA''R^9$ or $NCOOA''R^9$,
- 25 R^4 is H,
- X is methylene, ethylene, propylene or butylene,
- A'' and A''' are each, independently of one another, absent or alkylene having 1, 2, 3 or 4 carbon atoms,
- R^9 is H, $(CH_2)_n$ -aryl or $(CH_2)_n$ Het,
- 30 aryl is phenyl, naphthyl, fluorenyl or biphenyl, each of which is unsubstituted or monosubstituted by OR^{13} ,
- R^{13} is H or alkyl having 1-6 carbon atoms,

Het is pyridyl, pyridyl N-oxide, thienyl, furyl, pyrrolyl, pyridazinyl, pyrimidinyl, pyrazinyl, triazinyl, isoxazoliny, oxazoliny, thiazoliny, pyrazoliny, imidazoliny, naphthyl, quinoliny, isoquinoliny, cinnoliny, phthalazinyl, quinazoliny or quinoxaliny,
 5 B is phenyl which is unsubstituted or monosubstituted by OR¹³, N(R¹³)₂, O-alkylene-N(R¹³)₂ or O-alkylene-OH, or unsubstituted pyridyl.

and pharmaceutically usable derivatives, solvates and stereoisomers thereof, including mixtures thereof in all ratios.

10

12. Compounds according to one or more of Claims 1-11, in which

R¹ and R² are each, independently of one another, methoxy, ethoxy, propoxy or isopropoxy,

15 R³ is H, fluorenylmethyloxycarbonyl, acetyl, tert-butyloxycarbonyl, benzyloxycarbonyl, N,N-dimethylaminoethyl, benzyl or pyridylmethyl,

R⁴ is H,

X is methylene, ethylene, propylene or butylene,

20 R¹³ is H or alkyl having 1-6 carbon atoms,

Het is pyridyl,

B is phenyl which is unsubstituted or monosubstituted by OR¹³, N(R¹³)₂, O-alkylene-N(R¹³)₂ or O-alkylene-OH, or unsubstituted pyridyl;

25 and pharmaceutically usable derivatives, solvates and stereoisomers thereof, including mixtures thereof in all ratios.

13. Compounds of the formula I according to Claim 1 from the group consisting of

- 30 a) benzyl {1-(1S)-(4-tert-butoxybenzyl)-2-[3-(3-ethoxy-4-methoxyphenyl)-5,6-dihydro-4H-pyridazin-1-yl]-2-oxoethyl}carbamate,
 b) benzyl {2-[3-(3-ethoxy-4-methoxyphenyl)-5,6-dihydro-4H-pyridazin-1-yl]-1-(1S)-(4-hydroxybenzyl)-2-oxoethyl}carbamate,

- c) 2-(2S)-amino-1-[3-(3-ethoxy-4-methoxyphenyl)-5,6-dihydro-4H-pyridazin-1-yl]-3-[4-(2-hydroxyethoxy)phenyl]propan-1-one,
- d) 3-[4-(2-dimethylaminoethoxy)phenyl]-2-(2S)-(2-dimethylaminoethylamino)-1-[3-(3-ethoxy-4-methoxyphenyl)-5,6-dihydro-4H-pyridazin-1-yl]propan-1-one,
- 5 e) 2-(2S)-amino-3-[4-(2-dimethylaminoethoxy)phenyl]-1-[3-(3-ethoxy-4-methoxyphenyl)-5,6-dihydro-4H-pyridazin-1-yl]propan-1-one,
- f) 9H-fluoren-9-ylmethyl {1-(1S)-(4-tert-butoxybenzyl)-2-[3-(3-ethoxy-4-methoxyphenyl)-5,6-dihydro-4H-pyridazin-1-yl]-2-oxoethyl}carbamate,
- 10 g) 2-(2S)-amino-3-(4-tert-butoxyphenyl)-1-[3-(3-ethoxy-4-methoxyphenyl)-5,6-dihydro-4H-pyridazin-1-yl]propan-1-one,
- h) 2-(2S)-amino-1-[3-(3-ethoxy-4-methoxyphenyl)-5,6-dihydro-4H-pyridazin-1-yl]-3-(4-hydroxyphenyl)propan-1-one,
- 15 i) 2-(2S)-benzylamino-1-[3-(3-ethoxy-4-methoxyphenyl)-5,6-dihydro-4H-pyridazin-1-yl]-3-(4-hydroxyphenyl)propan-1-one,
- j) 1-[3-(3-ethoxy-4-methoxyphenyl)-5,6-dihydro-4H-pyridazin-1-yl]-3-(4-hydroxyphenyl)-2-(2S)-[(pyridin-4-ylmethyl)amino]propan-1-one,
- 20 k) tert-butyl {1-(1R)-(4-methoxybenzyl)-2-[3-(3-ethoxy-4-methoxyphenyl)-5,6-dihydro-4H-pyridazin-1-yl]-2-oxoethyl}carbamate,
- l) tert-butyl {1-(1S)-(4-methoxybenzyl)-2-[3-(3-ethoxy-4-methoxyphenyl)-5,6-dihydro-4H-pyridazin-1-yl]-2-oxoethyl}carbamate,
- m) N-{1-(1S)-(4-tert-butoxybenzyl)-2-[3-(3-ethoxy-4-methoxyphenyl)-5,6-dihydro-4H-pyridazin-1-yl]-2-oxoethyl}acetamide,
- 25 n) N-[2-[3-(3-ethoxy-4-methoxyphenyl)-5,6-dihydro-4H-pyridazin-1-yl]-1-(1S)-(4-hydroxybenzyl)-2-oxoethyl]acetamide,
- o) tert-butyl {2-[3-(3-ethoxy-4-methoxyphenyl)-5,6-dihydro-4H-pyridazin-1-yl]-2-oxo-1-(1R)-(pyridin-3-ylmethyl)ethyl}carbamate,
- 30 p) 2-(2R)-amino-1-[3-(3-ethoxy-4-methoxyphenyl)-5,6-dihydro-4H-pyridazin-1-yl]-3-pyridin-3-ylpropan-1-one,
- q) tert-butyl {2-[3-(3-ethoxy-4-methoxyphenyl)-5,6-dihydro-4H-pyridazin-1-yl]-2-oxo-1-(1R)-(pyridin-4-ylmethyl)ethyl}carbamate,

- r) 2-(2R)-amino-1-[3-(3-ethoxy-4-methoxyphenyl)-5,6-dihydro-4H-pyridazin-1-yl]-3-pyridin-4-ylpropan-1-one,
and pharmaceutically usable derivatives, solvates and stereoisomers thereof, including mixtures thereof in all ratios.

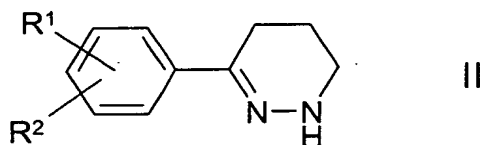
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14. Compounds of the formula I according to one or more of Claims 1 to 13 as phosphodiesterase IV inhibitors.

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15. Process for the preparation of compounds of the formula I and salts and solvates thereof, characterised in that

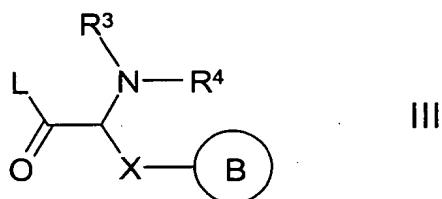
- a) a compound of the formula II



in which

15

R^1 and R^2 are as defined in Claim 1,
is reacted with a compound of the formula III



in which

20

L is Cl, Br, I or a free or reactively functionally modified OH group,
and R^3 , R^4 , X and B are as defined in Claim 1,
with the proviso that any further OH and/or amino group present is protected,
and subsequently, if desired, a protecting group is removed,

25

or

b) one or more radicals R^1 , R^2 , R^3 , R^4 and/or B in a compound of the formula I are converted into one or more other radicals R^1 , R^2 , R^3 , R^4 and/or B by

- i) cleaving an ether or ester,
- 5 ii) alkylating or acylating an OH function,
- iii) reductively alkylating an amino group,

and/or in that a basic compound of the formula I is converted into one of its salts by treatment with an acid.

10

16. Medicaments comprising at least one compound of the formula I according to one or more of Claims 1 to 13 and/or pharmaceutically usable derivatives, solvates and stereoisomers thereof, including mixtures thereof in all ratios, and, if desired, excipients and/or adjuvants.

15

17. Use of compounds of the formula I according to one or more of Claims 1 to 13 and/or physiologically acceptable salts or solvates thereof for the preparation of a medicament for the treatment of a patient suffering from a disease or condition mediated by the PDE IV isozyme in its role in regulating the activation and degranulation of human eosino-

20

phils.

18. Use according to Claim 17 of compounds of the formula I according to one or more of Claims 1 to 13 and/or physiologically acceptable salts or solvates thereof for the preparation of a medicament for combat-

25

ing allergic diseases, asthma, chronic bronchitis, atopic dermatitis, psoriasis and other skin diseases, inflammatory diseases, autoimmune diseases, such as, for example, rheumatoid arthritis, multiple sclerosis, Crohn's disease, diabetes mellitus or ulcerative colitis, osteoporosis, transplant rejection reactions, cachexia, tumour growth or tumour meta-

30

stases, sepsis, memory disorders, atherosclerosis and AIDS.

19. Use according to Claim 17 or 18 of a compound of the formula I according to Claims 1 to 13 for the preparation of a medicament for the treatment or prevention of one or more of the diseases, pathological disorders and conditions from the following group:

5 asthma of whatever type, etiology or pathogenesis, or asthma selected from the group consisting of atopic asthma, non-atopic asthma, allergic asthma, atopic, IgE-mediated asthma, bronchial asthma, essential asthma, true asthma, intrinsic asthma caused by pathophysiological disturbances, extrinsic asthma caused by environmental factors, essential
10 asthma of unknown or inapparent cause, non-atopic asthma, bronchitic asthma, emphysematous asthma, exercise-induced asthma, occupational asthma, infective asthma caused by bacterial, fungal, protozoal or viral infection, non-allergic asthma, incipient asthma, wheezy infant syndrome; chronic or acute bronchoconstriction, chronic bronchitis, small air-
15 way obstruction and emphysema;

 obstructive or inflammatory airway disease of whatever type, etiology or pathogenesis, or an obstructive or inflammatory airway disease selected from the group consisting of asthma; pneumoconiosis, chronic eosinophilic pneumonia; chronic obstructive pulmonary disease (COPD),
20 COPD including chronic bronchitis, pulmonary emphysema or dyspnoea associated therewith, COPD that is characterised by irreversible, progressive airway obstruction, acute respiratory distress syndrome (ARDS), and exacerbation of airway hypersensitivity consequent to other medication therapy;

25 pneumoconiosis of whatever type, etiology or pathogenesis, or pneumoconiosis selected from the group consisting of aluminosis, anthracosis (asthma), asbestosis, chalicosis, ptilosis caused by inhaling the dust from ostrich feathers, siderosis caused by the inhalation of iron particles, silicosis, byssinosis or cotton-dust pneumoconiosis and talc pneumoconiosis;
30

 bronchitis of whatever type, etiology or pathogenesis, or bronchitis selected from the group consisting of acute bronchitis, acute laryngo-tracheal bronchitis, arachidic bronchitis, catarrhal bronchitis, croupus

bronchitis, dry bronchitis, infectious asthmatic bronchitis, productive bronchitis, staphylococcal or streptococcal bronchitis; and vesicular bronchitis;

5 bronchiectasis of whatever type, etiology or pathogenesis, or bronchiectasis selected from the group consisting of cylindric bronchiectasis, sacculated bronchiectasis, fusiform bronchiectasis, capillary bronchiectasis, cystic bronchiectasis, dry bronchiectasis and follicular bronchiectasis;

10 seasonal allergic rhinitis, perennial allergic rhinitis, or sinusitis of whatever type, etiology or pathogenesis, or sinusitis selected from the group consisting of purulent or nonpurulent sinusitis, acute or chronic sinusitis, and ethmoid, frontal, maxillary, or sphenoid sinusitis;

15 rheumatoid arthritis of whatever type, etiology or pathogenesis, or rheumatoid arthritis selected from the group consisting of acute arthritis, acute gouty arthritis, primary chronic arthritis, osteoarthritis, infectious arthritis, Lyme arthritis, progressive arthritis, psoriatic arthritis and spondylarthritis;

gout, and fever and pain associated with inflammation;

20 an eosinophil-related pathological disorder of whatever type, etiology or pathogenesis, or an eosinophil-related pathological disorder selected from the group consisting of eosinophilia, pulmonary infiltration eosinophilia, Löffler's syndrome, chronic eosinophilic pneumonia, tropical pulmonary eosinophilia, bronchopneumonic aspergillosis, aspergilloma, eosinophilic granuloma, allergic granulomatous angiitis or Churg-Strauss syndrome, polyarteritis nodosa (PAN) and systemic necrotising vasculitis;

25 atopic dermatitis, allergic dermatitis, or allergic or atopic eczema;

30 urticaria of whatever type, etiology or pathogenesis, or urticaria selected from the group consisting of immune-mediated urticaria, complement-mediated urticaria, urticariogenic material-induced urticaria, physical stimulus-induced urticaria, stress-induced urticaria, idiopathic urticaria, acute urticaria, chronic urticaria, angioedema, cholinergic urticaria, cold urticaria in the autosomal dominant form or in the acquired form, contact urticaria, giant urticaria and papular urticaria;

conjunctivitis of whatever type, etiology or pathogenesis, or conjunctivitis selected from the group consisting of actinic conjunctivitis, acute catarrhal conjunctivitis, acute contagious conjunctivitis, allergic conjunctivitis, atopic conjunctivitis, chronic catarrhal conjunctivitis, purulent conjunctivitis and vernal conjunctivitis;

uveitis of whatever type, etiology or pathogenesis, or uveitis selected from the group consisting of inflammation of all or part of the uvea, anterior uveitis, iritis, cyclitis, iridocyclitis, granulomatous uveitis, nongranulomatous uveitis, phacoantigenic uveitis, posterior uveitis, chorioiditis and chorioretinitis;

psoriasis;

multiple sclerosis of whatever type, etiology or pathogenesis, or multiple sclerosis selected from the group consisting of primary progressive multiple sclerosis and relapsing remitting multiple sclerosis;

autoimmune/inflammatory diseases of whatever type, etiology or pathogenesis, or an autoimmune/inflammatory disease selected from the group consisting of autoimmune haematological disorders, haemolytic anaemia, aplastic anaemia, pure red cell anaemia, idiopathic thrombocytopenic purpura, systemic lupus erythematosus, polychondritis, scleroderma, Wegner's granulomatosis, dermatomyositis, chronic active hepatitis, myasthenia gravis, Stevens-Johnson syndrome, idiopathic sprue, autoimmune inflammatory bowel diseases, ulcerative colitis, Crohn's disease, endocrine ophthalmopathy, Basedow's disease, sarcoidosis, alveolitis, chronic hypersensitivity pneumonitis, primary biliary cirrhosis, juvenile diabetes or type 1 diabetes mellitus, anterior uveitis, granulomatous or posterior uveitis, keratoconjunctivitis sicca, epidemic keratoconjunctivitis, diffuse interstitial pulmonary fibrosis or interstitial pulmonary fibrosis, pulmonary cirrhosis, cystic fibrosis, psoriatic arthritis, glomerulonephritis with and without nephrotic syndrome, acute glomerulonephritis, idiopathic nephrotic syndrome, minimal change nephropathy, inflammatory/ hyperproliferative skin diseases, psoriasis, atopic dermatitis, contact dermatitis, allergic contact dermatitis, benign familial pemphigus, pemphigus erythematosus, pemphigus foliaceus and pemphigus vulgaris;

prevention of foreign transplant rejection following organ transplantation;

inflammatory bowel disease (IBD) of whatever type, etiology or pathogenesis, or inflammatory bowel disease selected from the group consisting of ulcerative colitis (UC), collagenous colitis, colitis polyposa, 5 transmural colitis and Crohn's disease (CD);

septic shock of whatever type, etiology or pathogenesis, or septic shock selected from the group consisting of renal failure, acute renal failure, cachexia, malarial cachexia, hypophysial cachexia, uremic cachexia, 10 cardiac cachexia, cachexia suprarenalis or Addison's disease, cancerous cachexia, and cachexia as a consequence of infection by the human immunodeficiency virus (HIV);

liver damage;

pulmonary hypertension and hypoxia-induced pulmonary hyper- 15 tension;

bone loss diseases, primary osteoporosis and secondary osteoporosis;

pathological disorders of the central nervous system of whatever type, etiology or pathogenesis, or a pathological disorder of the central nervous system selected from the group consisting of depression, Parkinson's disease, learning and memory disorders, tardive dyskinesia, drug 20 dependence, arteriosclerotic dementia, and dementias that accompany Huntington's chorea, Wilson's disease, paralysis agitans and thalamic atrophies;

infections, especially viral infections, where these viruses 25 increase the production of $\text{TNF-}\alpha$ in their host or where these viruses are sensitive to up-regulation of $\text{TNF-}\alpha$ in their host so that their replication or other vital activities are adversely affected, including viruses selected from the group consisting of HIV-1, HIV-2 and HIV-3, cytomegalovirus, CMV, 30 influenza, adenoviruses and Herpes viruses, including Herpes zoster and Herpes simplex;

yeast and fungal infections, where these yeasts and fungi are sensitive to up-regulation by TNF- α or elicit TNF- α production in their host, for example fungal meningitis, particularly when administered in conjunction with other medicaments of choice for the treatment of systemic yeast and fungal infections, including, but not limited to, polymycins, for example polymycin B, imidazoles, for example clotrimazole, econazole, miconazole and ketoconazole, triazoles, for example fluconazole and itranazole, and amphotericins, for example amphotericin B and liposomal amphotericin B;

ischaemia-reperfusion damage, autoimmune diabetes, retinal autoimmunity, chronic lymphocytic leukaemia, HIV infections, lupus erythematosus, kidney and ureter diseases, pathological urogenital and gastrointestinal disorders and prostate diseases.

20. Use according to Claim 17, 18 or 19 of a compound of the formula I according to Claims 1 to 13 for the preparation of a medicament for the treatment of (1) inflammatory diseases and conditions, including joint inflammation, rheumatoid arthritis, rheumatoid spondylitis, osteoarthritis, inflammatory bowel disease, ulcerative colitis, chronic glomerulonephritis, dermatitis and Crohn's disease; (2) airway diseases and conditions, including asthma, acute respiratory distress syndrome, chronic pulmonary inflammatory disease, bronchitis, chronic obstructive airway disease and silicosis; (3) infectious diseases and conditions, including sepsis, septic shock, endotoxic shock, Gram-negative sepsis, toxic shock syndrome, fever and myalgia due to bacterial, viral or fungal infections, and influenza; (4) immune diseases and conditions, including autoimmune diabetes, systemic lupus erythematosus, GvH reaction, rejection of foreign transplants, multiple sclerosis, psoriasis and allergic rhinitis; and (5) other diseases and conditions, including bone absorption diseases, reperfusion damage, cachexia secondary to infection or malignancy, cachexia secondary to AIDS, human immunodeficiency virus (HIV) infection, or AIDS related complex (ARC), keloid formation, scar tissue formation, type 1 diabetes mellitus, and leukaemia.

21. Use according to Claim 17 of a compound of the formula I according to Claims 1 to 13 for the preparation of a medicament for the treatment of myocardial diseases.

22. Use according to Claim 21 of a compound of the formula I according to Claims 1 to 13 for the preparation of a medicament for the treatment of myocardial diseases, where these myocardial diseases have inflammatory and immunological properties.

23. Use according to Claim 17 of a compound of the formula I according to Claims 1 to 13 for the preparation of a medicament for the treatment of coronary heart disease, reversible or irreversible myocardial ischaemia/reperfusion damage, acute or chronic heart failure and restenosis, including in-stent restenosis and stent-in-stent restenosis.

24. Combination of a compound according to Claims 1 to 13 together with one or more members of the following group:

(a) leukotriene biosynthesis inhibitors: 5-lipoxygenase (5-LO) inhibitors and 5-lipoxygenase activating protein (FLAP) antagonists selected from the group consisting of zileuton, ABT-761, fenleuton, tepoxalin, Abbott-79175, Abbott-85761, N-(5-substituted) thiophene-2-alkylsulfonamides, 2,6-di-tert-butylphenol hydrazones, Zeneca ZD-2138, SB-210661, the pyridinyl-substituted 2-cyanonaphthalene compound L-739,010, the 2-cyanoquinoline compound L-746,530, the indole and quinoline compounds MK-591, MK-886 and BAY x 1005;

(b) receptor antagonists for the leukotrienes LTB₄, LTC₄, LTD₄ and LTE₄ selected from the group consisting of the phenothiazin-3-one compound L-651,392, the amidino compound CGS-25019c, the benzoxazolamine compound ontazolast, the benzenecarboximideamide compound BIIL 284/260, the compounds zafirlukast, ablukast, montelukast, pranlu-

kast, verlukast (MK-679), RG-12525, Ro-245913, iralukast (CGP 45715A) and BAY x 7195;

(c) PDE IV inhibitors;

(d) 5-lipoxygenase (5-LO) inhibitors; 5-lipoxygenase activating protein (FLAP) antagonists;

(e) dual inhibitors of 5-lipoxygenase (5-LO) and antagonists of platelet activating factor (PAF);

(f) leukotriene antagonists (LTRAs), including LTB₄, LTC₄, LTD₄ and LTE₄ antagonists;

(g) antihistamine H₁ receptor antagonists, including cetirizine, loratadine, desloratadine, fexofenadine, astemizole, azelastine and chlorpheniramine;

(h) gastroprotective H₂ receptor antagonists;

(i) α_1 - and α_2 -adrenoreceptor agonist vasoconstrictor sympathomimetic agents administered orally or topically for decongestant use, selected from the group consisting of propylhexedrine, phenylephrine, phenylpropanolamine, pseudoephedrine, naphazoline hydrochloride, oxymetazoline hydrochloride, tetrahydrozoline hydrochloride, xylometazoline hydrochloride and ethylnorepinephrine hydrochloride;

(j) one or more α_1 - and α_2 -adrenoreceptor agonists as listed above under (i) in combination with one or more inhibitors of 5-lipoxygenase (5-LO) as listed above under (a);

(k) anticholinergic agents, including ipratropium bromide, tiotropium bromide, oxitropium bromide, pirenzepine and telenzepine;

- (l) β_1 - to β_4 -adrenoreceptor agonists selected from the group consisting of metaproterenol, isoproterenol, isoprenaline, albuterol, salbutamol, formoterol, salmeterol, terbutaline, orciprenaline, bitolterol and pirbuterol;
- 5 (m) theophylline and aminophylline;
- (n) sodium cromoglycate;
- 10 (o) muscarinic receptor (M1, M2 and M3) antagonists;
- (p) COX-1 inhibitors (NSAIDs) and nitric oxide NSAIDs;
- (q) the COX-2 selective inhibitor rofecoxib;
- 15 (r) insulin-like growth factor type I (IGF-1) mimetics;
- (s) ciclesonide;
- 20 (t) inhalation glucocorticoids with reduced systemic side effects selected from the group consisting of prednisone, prednisolone, flunisolide, triamcinolone acetonide, beclomethasone dipropionate, budesonide, fluticasone propionate and mometasone furoate;
- 25 (u) tryptase inhibitors;
- (v) platelet activating factor (PAF) antagonists;
- (w) monoclonal antibodies against endogenous inflammatory entities;
- 30 (x) IPL 576;

- (y) antitumour necrosis factor (TNF α) agents selected from the group consisting of etanercept, infliximab and D2E7;
- (z) DMARDs selected from the group consisting of leflunomide;
- 5 (aa) TCR peptides;
- (bb) interleukin converting enzyme (ICE) inhibitors;
- 10 (cc) IMPDH inhibitors;
- (dd) adhesion molecule inhibitors, including VLA-4 antagonists;
- (ee) cathepsins;
- 15 (ff) MAP kinase inhibitors;
- (gg) glucose 6-phosphate dehydrogenase inhibitors;
- 20 (hh) kinin B₁ and B₂ receptor antagonists;
- (ii) gold in the form of an aurothio group together with various hydrophilic groups;
- 25 (jj) immunosuppressive agents selected from the group consisting of cyclosporine, azathioprine and methotrexate;
- (kk) anti-gout agents selected from the group consisting of colchicines;
- 30 (ll) xanthine oxidase inhibitors selected from the group consisting of allopurinol;

(mm) uricosuric agents selected from the group consisting of probenecide, sulfinpyrazone and benzbromarone;

5 (nn) antineoplastic agents, which are antimitotic medicaments selected from the group consisting of vinblastine and vincristine;

(oo) agents for promoting growth hormone secretion;

10 (pp) inhibitors of matrix metalloproteases (MMPs) selected from the group consisting of stromelysins, collagenases, gelatinases, aggrecanase, collagenase-1 (MMP-1), collagenase-2 (MMP-8), collagenase-3 (MMP-13), stromelysin-1 (MMP-3), stromelysin-2 (MMP-10) and stromelysin-3 (MMP-11);

15 (qq) transforming growth factor (TGF β);

(rr) platelet-derived growth factor (PDGF);

20 (ss) fibroblast growth factor selected from the group consisting of basic fibroblast growth factor (bFGF);

(tt) granulocyte macrophage colony stimulating factor (GM-CSF);

25 (uu) capsaicin;

(vv) tachykinin NK₁ and NK₃ receptor antagonists selected from the group consisting of NKP-608C; SB233412 (talnetant) and D-4418;

30 (ww) elastase inhibitors selected from the group consisting of UT-77 and ZD-0892;

and

(xx) adenosine A2a receptor agonists.

25. Medicaments comprising at least one compound of the formula I according to one or more of Claims 1 to 13 and/or pharmaceutically
5 usable derivatives, solvates and stereoisomers thereof, including mixtures thereof in all ratios, and at least one further medicament active ingredient.

26. Set (kit) consisting of separate packs of
(a) an effective amount of a compound of the formula I according to one
10 or more of Claims 1 to 13 and/or pharmaceutically usable derivatives, solvates and stereoisomers thereof, including mixtures thereof in all ratios, and
(b) an effective amount of a further medicament active ingredient.